REMARKS

On page 2 of the final Office Action dated April 20, 2009, the Examiner noted the presence of typographical errors rendering a few sentences unreadable in the "Remarks" section of the Amendment filed March 24, 2009. Applicants appreciate the Examiner's entry of this amendment and her efforts to examine the case despite the noted errors. It is believed that the errors were machine-generated errors associated with scanning and/or electronic filing of the response.

To clarify and complete the record, Applicants are submitting herewith a **courtesy copy** of the "Remarks" section only of the Amendment of March 24, 2009, that does not contain the noted errors. This submission is only a **courtesy copy** to clarify the arguments in the "Remarks" section of the prior response. It is not intended to replace or remove the previous response of record.

On September 25, 2009, the examiner contacted Applicants' attorney by telephone to discuss the application. During the conversation, the examiner noted her intention to issue an Advisory Action maintaining the rejections in reply to the After Final Response filed on September 21, 2009. The examiner indicated that she was not persuaded by the arguments in the After Final Response.

However, she acknowledged that there is probably patentable subject matter in the application, but not in the current claims as written. The examiner noted the long prosecution history of this case and she suggested filing a Request for Continued Examination (RCE), to provide an opportunity to further study the issues and to hold an interview to expedite prosecution.

As suggested by the examiner, Applicants have filed an RCE concurrently herewith to withdraw finality and allow for an interview. Applicants are in the process of scheduling the interview and respectfully ask the examiner to wait to act on the case until after the interview.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Favorable action is solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /jfw/
Jay F. Williams
Registration No. 48,036

JFW:jhw
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\I\inl2\WALLACH33\PTO\2009-10-16SupplementalResponse.doc

APPENDIX:

The Appendix includes the following item(s):

courtesy copy of the "Remarks" section of the Amendment

filed March 24, 2009

REMARKS

Claims 20, 25, 69, 70, 72, 75, 82-91, 100 and 102-105 presently appear in this case. Claims 20-25, 68, 72, 79, 84, 94 and 99 have been withdrawn from consideration. No claims have been allowed. The Official Action of September 25, 2008, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to the use of NIK and related molecules for binding to cγc and inhibiting cγc/NIK interaction, thus modulating signal activities controlled by cytokines and NIK induced NF-κB activation, and thereby treating diseases in which NIK/cγc interaction is involved or in which NF-κB activation is involved.

The examiner states that applicant's arguments that claims 20 and 24 are generic have not been accepted as the elected species is IL-2 and these claims exclude IL-2. Nevertheless, it is urged that once generic claim 69 is allowed, the examiner should examine claims 20 and 25 as they are not patentably distinct from generic claim 69. Furthermore, they should be examined since the have already been searched and examined previously. Note that even when claims are restrictable, they may be examined together if doing so would not create significant additional burden on the part of the examiner. Furthermore, once the generic claims 69

and 70 are examined and found allowable, regardless of whether or not they are considered patentably distinct from claim 20, it would not require any additional burden to examine claim 20 in this application.

For all of these reasons, claims 20 and 24, particularly as presently amended, should be rejoined and examined upon examination and allowance of the full scope of claims 69 and 70.

Claims 66, 67, 69, 70, 73-78, 80-83, 85-88, 90-93, 95-98, 100 and 101 are objected to for reciting non-elected subject matter, there being no allowable generic or linking claim.

Notwithstanding this objection, these claims are being left to remain in the case as it is believed that the elected species have now been shown to be allowable and, therefore, the full scope of the generic or linking claims should now be rejoined and examined in this case.

Claim 66, 69, 70, 73 and 76 have been objected to for poor grammar. The examiner suggests language that he likes better.

While applicant denies that the previous language contained any improper grammar, these claims have now been amended to accept the examiner's language. However, for

future reference, the examiner's attention is invited to MPEP 2173.02, where it states:

> The examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph, is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. When the examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the examiner that the claims are directed to such patentable subject matter, he or she should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire. Examiners are encouraged to suggest claim language to applicants to improve the clarity or precision of the language used, but should not reject claims or insist on their own preferences if other modes of expression selected by applicants satisfy the statutory requirement.

Claim 66, line 3 has been objected to for "activation of a cytokine." The examiner states that this should be "activation of a cytokine receptor."

Claim 66 has now been deleted, thus obviating this objection.

Claims 66, 67, 69, 70, 73-78, 80-83, 85-88, 90-93, 95-98, 100 and 101 have been rejected under 35 USC 112, second paragraph, as being indefinite. The examiner states that the phrase "maintains at least… second identity" is indefinite and

the examiner suggests use of the term "has at least… sequence identity."

All of these claims have now been amended to accept the examiner's suggested language, thus obviating this part of the rejection.

Claims 66, 69, 70, 73, 76, 77, 82, 87, 92 and 97 have been objected to with respect to the phrase "pharmaceutically acceptable functional derivative." The examiner states that this language renders the claim indefinite. The examiner states that the disclosure at page 24, paragraph 2, is only exemplary and the skilled artisan would not know the metes and bounds of the recited invention. This part of the rejection is respectfully traversed.

Those of ordinary skill in the art are well aware that polypeptides may be derivatized without affecting the activity of the polypeptide and without imparting toxicity to the pharmaceutical composition. This is commonly done to improve pharmacological properties, such as solubility, cell permeability, therapeutic half life, etc., for example. While the last sentence of the first full paragraph on page 24 has examples, the first sentence of this paragraph is not exemplary but is definitional. The fact that the claim is broad does not affect its definiteness. As stated in MPEP 2173.04:

> Breadth of a claim is not to be equated with indefiniteness... If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 USC 112, second paragraph.

As the examiner has not alleged that the scope of the subject matter embraced by the claims is unclear, nor that applicants have intended that the invention be of a scope different from that defined in the claims, an indefiniteness rejection is improper. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

Claims 67, 74, 75, 77, 78, 80-83, 85-88, 90-93, 95, 98, 100 and 101 are considered indefinite because the first word of the claim is "A" rather than "The."

While applicants strongly disagree with the examiner's suggestion that the previous claim language was indefinite or had improper antecedent usage, nevertheless, in order to obviate this objection, the claims have been amended as suggested by the examiner.

Claims 66, 67, 69, 70, 73-78, 80-83, 85-88, 90-93, 95-98, 100 and 101 have been rejected under 35 USC 112, first paragraph, for lack of enablement. The examiner states that the claims encompass treating any known or unknown disease mediated by activating any cytokine receptor comprising cγc, wherein the treating is with a NIK polypeptide. The examiner states that

neither the specification nor the prior art teach (i) all known or unknown cytokine receptors comprising a cγc, (ii) that all effects activating a cytokine receptor comprising a cγc are mediated by cγc/NIK binding or NIK activation, (iii) all known and unknown diseases affected by a cytokine receptor comprising a cγc, or (iv) any disease that can be treated using an NIK polypeptide that binds to cγc and inhibits cγc/NIK binding. This rejection is respectfully traversed.

Claim 66 and all those dependent therefrom have now been deleted in order to obviate the part of the rejection relating to which cytokine receptors have the cγc and whether or not all the effects of activating a cytokine receptor comprising a cγc are mediated by cγc/NIK binding or NIK activation. Claim 69 defines the disease as being one "in which NF-κB inducing kinase (NIK) and cγc interaction is involved in the pathogenesis of said disease." As it has been shown in the present specification that the polypeptides used in the present method interfere with NIK/cγc interaction, the type of disease that can be treated in accordance with the present invention is adequately defined in claim 69. There is no reason to believe that any disease in which NIK/cγc interaction is involved in the pathogenesis thereof would not be treatable by means of the present invention. Certainly, the examiner has not met his burden to establish a reasonable basis to

question the enablement provided for the claimed invention. See MPEP 2164.04, particularly where it states:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. … [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

The examiner states that he fails to see where the background section of the specification describes how the prior art teaches that binding of cγc/NIK affects any specific disease. The examiner requests that applicant submit an IDS with references containing any such teachings. With respect thereto, the examiner's attention is respectfully invented to the specification beginning at page 5, line 16, through page 7, line 15. There, it discloses that activation of the NF-κB pathway is involved in the pathogenesis of many specified diseases. The experimentation in the present specification establishes that cγc and NIK interaction induces NF-κB activation and that inhibition of cγc/NIK

interaction inhibits NIK mediated NF-κB activation. See, for example, page 20, line 9, up to page 21, line 4, and all of the examples in the present specification. Thus, all of those diseases mediated by NF-κB are necessarily diseases in which NIK and cγc interaction is involved in the pathogenesis of the disease. Accordingly, there is enabling support in the specification for the treatment of such diseases by the polypeptides as defined in claim 69.

The same is true with respect to claim 70, which is directed to treatment of a disease "in which NF-κB activation is involved." Again, the background of the specification at page 5, line 16, through page 7, line 15, is specifically directed to diseases in which NF-κB activation is involved. The examiner has not explained why those of ordinary skill in the art could not treat any such disease by means of the present invention without undue experimentation.

In order to reduce the issues for appeal and in an attempt to place the case in condition for allowance, claims 73, 76, and those claims ultimately dependent therefrom have now been deleted. Furthermore, withdrawn claim 20 has been amended to use the preamble language of claim 69. Additionally, reference to prevention has been deleted from all of the claims. Thus, all of the present claims are directed either to a method of treating a disease in which NIK and cγc interaction is involved in the

pathogenesis of the disease or a disease in which NF-κB activation is involved. As discussed above, the specification discusses many such diseases.

All of the references discussed in the specification, as well as those cited during the international search and examination, have now been submitted in an IDS. As explained in MPEP 2164.04 and as discussed above, the burden is on the examiner to establish a reasonable basis to question the enablement provided in the claimed invention. Further this section of the MPEP concludes with the admonition that the examiner should always look for enabled, allowable subject matter and communicate to applicant what that subject matter is at the earliest point possible in the prosection of the application. The examiner has not done that here.

Accordingly, at least with respect to the diseases that can be treated by means of the present invention, reconsideration and withdrawal of this part of this part of the rejection is respectfully urged.

As to the examiner's comments that the claims are still too broad with respect to functional derivatives, this part of the rejection is respectfully traversed. As discussed above with respect to the indefiniteness rejection, the description of functional derivates in the specification makes clear that there it is a derivative of a functional group on the polypeptide that

does not change the biological properties of the polypeptide. An analysis of the *Wands* factors will show that those of ordinary skill in the art have very high degree of knowledge in the field. Those who formulate pharmaceutical compositions with polypeptides are well aware of many ways to derivatize a polypeptide without changing its activity in order to improve pharmacological properties for example. It is well within the skill of those of ordinary skill in the art, without engaging undue experimentation, to make any such derivative and, if necessary, to test them to see that the compound maintains its activity as is required by the claims. Applicants should be entitled to some degree of breadth in defining their invention. A person who invents the use of a polypeptide should not give free reign to an infringer who derivatizes it in a known manner in order to improve solubility, for example. The examiner has not explained why it would take undue experimentation to determine whether any given derivative falls within the scope of the claim.

The examiner's attention is directed to new claims 102 and 104, which specify that the functional derivatives are an ester or aliphatic amide of a carboxyl group and N-acyl derivative of a free amino group, or an O-acyl derivative of a free hydroxyl group. This is supported by the specification in the first paragraph of page 24. These claims should be free of this part of the rejection.

Furthermore, separate consideration should be given to new claims 103 and 105, which exclude function derivatives altogether.

For all of these reasons, reconsideration and withdrawal of this rejection is respectfully urged.

Claims 66, 67, 69, 70 and 73-76 have been rejected under 35 USC 112, first paragraph, written description. The examiner states that applicant's arguments have not been found to be persuasive for the reasons explained in (a). In other words, it appears that the only objection that the examiner now has to the claims from the standpoint of written description relates to the term "functional derivative." This rejection is respectfully traversed.

First of all, the present rejection is not applicable to new claims 103 and 105. It is requested that the examiner acknowledge this fact.

Furthermore, new claims 102 and 104 have specific language as to what the derivatives are. It is urged that these claims are also free of the written description rejection.

As to the remaining claims, those of ordinary skill in the art would understand that applicants were in possession of the full scope of the functional derivates subparagraph of the independent claims as functional derivatives of active polypeptides are extremely well known in the art. Applicant has

made no new discoveries with respect to functional derivatives but is merely claiming its polypeptides in a scope so as to include such derivatives that are used, for example, to improve pharmacological properties. Reconsideration and withdrawal of this rejection is therefore also respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 USC 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /rlb/
Roger L. Browdy
Registration No. 25,618

RLB:jhw
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
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